

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

UMEK et al.

Application No. 09/626,096

Filed: July 26, 2000


For: Sequence Determination of Nucleic
Acids Using Electronic Detection

Examiner: CALAMITA, Heather

Art Unit: 1637 Conf. No.: 8157

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Monica E. Carlos

PREAPPEAL BRIEF REQUEST FOR REVIEW

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Sir:

In accordance with 1296 Off. Gaz. Pat. Office 67 (July 12, 2005), Applicants request review of the Final Rejection of February 7, 2008, in the above-identified application. This request includes no amendments, and a Notice of Appeal has been filed herewith. The undersigned is an attorney of record.

Rejection under 35 USC 103(a)

The Examiner has maintained the rejection of claims 60-69 under 35 USC 103(a) over Kayyem et al., PCT Publication WO/1998/020162, in view of Shuber, US Patent 5,633,134.

Kayyem and Shuber in combination do not teach or suggest to one of ordinary skill in the art all of the limitations of claims. In arguing to the contrary, the Examiner has committed clear errors of fact and thus has not properly resolved the scope and content of the cited references and the differences between the cited references and the claims. The Examiner also has not resolved the level of ordinary skill in the art. Furthermore, the Examiner has not provided the rationale necessary to support a conclusion of obviousness. Because the Examiner has not properly analyzed the Graham factors and

has not provided a reason for finding obviousness, the Examiner has not established a prima facie case of obviousness.

Kayyem and Shuber, by themselves or in combination, do not disclose all of the limitations of the claims. Claim 60 recites contacting an electrode with a first label probe comprising a first electron transfer moiety (ETM) with a **first redox potential** and a second label probe comprising a second ETM with a **second redox potential**. Kayyem and Shuber do not disclose this step.

In arguing that Kayyem teaches the limitation of a second ETM label with a second redox potential, the Examiner in the Final Rejection of February 7, 2008 ("Final Rejection") and the Advisory Action of May 1, 2008 ("Advisory Action"), cites Kayyem at page 52, lines 6-24, and states that "Kayyem teaches a first ETM label on a first oligonucleotide and a second ETM label on a second oligonucleotide." This is a clear error of fact. Kayyem, on page 52, lines 6 and 7, teaches "a first single stranded nucleic acid covalently attached to an **electrode** via a conductive oligomer and b) a second single stranded nucleic acid containing a second electron transfer moiety[.]" Thus, in this embodiment, there are two ETMs, the first ETM being an electrode, which does not function as a label. In contrast, claim 60 recites three ETMs: an electrode, a first ETM with a first redox potential and a second ETM with a second redox potential. In claim 60, the electrode is contacted with at least two label probes, each having an ETM with a distinct redox potential, whereas in the Kayyem embodiment, the electrode is contacted with one type of label probe having an ETM with one redox potential. Kayyem therefore does not teach all of the limitations of the claims.

In arguing that Shuber teaches the limitation of a second ETM with a second redox potential, the Examiner on page 5 of the Final Rejection states that "Shuber teaches a first step using multiple probes and if a positive result is present then in a second step a second probe is used to determine which mutation is present." Although Shuber applies multiple probes to a test nucleic acid, each of these probes is labeled in the same manner, that is, they are all ³²P labeled. If a particular pool of probes shows positive results, a second and possibly further rounds of testing involving the individual members of the **same** pool are required because the individual ³²P labeled probes result in the same type of signal that cannot distinguish the individual probes. See Shuber, col. 5-8. In contrast, claim 60 recites using at least two different label probes, each having an ETM with a unique, distinguishable redox potential. According to the claimed invention, a distinguishable signal will result, depending on which label probe hybridizes. In other words, Shuber teaches using multiple probes of different sequence but having the **same**,

indistinguishable label, while claim 60 recites using at least two probes of different sequence, each having a **unique, distinguishable** label. Shuber therefore does not teach all of the limitations of the claims.

The Examiner states on page 4 of the Final Rejection and in the Advisory Action that Shuber teaches a second ETM with a second redox potential because “Shuber teaches multiple oligonucleotide probes with labels.” However, merely teaching that multiple oligonucleotide probes can be used does not lead one of skill in the art to using at least two different label probes, each having an ETM with a unique, distinguishable redox potential. As discussed above, Shuber teaches that each probe has the same, indistinguishable label. The embodiment of Kayyem on page 52, lines 6-24, discloses using one type of label probe, and so, whether alone or combined with Shuber, does not provide a motivation to use at least two distinguishable label probes.

Thus, Shuber and Kayyem, alone or *in combination*, do not teach all of the limitations of the claims. By committing clear errors of fact in characterizing Shuber and Kayyem, the Examiner has failed to properly analyze the scope and content of the cited references and to ascertain the differences between the claimed invention and the cited references. Applicants further note that nowhere in the record has the Examiner resolved the level of ordinary skill in the art. The Examiner has therefore failed to properly analyze all three Graham factors as required by *KSR Int’l. Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), and thus has not established a *prima facie* case of obviousness.

In addition to analyzing the Graham factors, *KSR* at page 1741 requires “some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” Here, the Examiner states that “an ordinary practitioner would have been motivated to use ETM labeled oligonucleotides, as taught by Kayyem et al. with the multiple oligonucleotide probes for mutation detection because Kayyem states that no electron transfer occurs unless nucleotide base pairing exists in the double stranded sequence between the electron donor and acceptor.” First, the Examiner has never made clear how one of skill in the art would “use” ETM labeled oligonucleotides “with” the multiple oligonucleotide probes. Second, combining “ETM labeled oligonucleotides” with “multiple oligonucleotide probes for mutation detection” does not follow from the reason cited by the Examiner. The motivation stated by the Examiner merely suggests that some sort of hybridization must occur for there to be electron transfer. On this reason alone, it is not at all clear why one of skill in the art would apply to an electrode multiple probes of different sequence as taught by Shuber to a target sequence when a single probe would suffice to achieve the hybridization necessary for electron transfer. It is even less

clear why, based on the reason cited by the Examiner, one of skill in the art would apply to an electrode multiple probes of different sequence, each having an ETM with a unique, distinguishable redox potential, since as discussed above, Shuber and Kayyem in combination do not teach or suggest using at least two label probes wherein each is labeled with an ETM having a unique, distinguishable redox potential. The Examiner has thus failed to provide the reasoning necessary to support the legal conclusion of obviousness.

The Examiner has not carried the burden of making a proper factual inquiry according to the Graham factors and providing articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. The Examiner has thus failed to establish a prima facie case of obviousness. Withdrawal of the rejection is therefore respectfully requested.

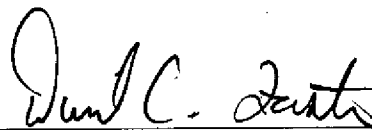
Conclusion

In view of the foregoing, it is believed that all claims now pending in this application are in condition for allowance.

Authorization is granted to charge any outstanding fees dues at this time for the continued prosecution of this matter to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 (Client-Matter No. 067456-5030-US).

Respectfully submitted,

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